UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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Palliative Care Pharmacy Team:

Guest Author:
Hyunwoo Kim, 4th Year Student Pharmacist at University of Pittsburgh School of Pharmacy

Clinical Pharmacy Specialist:

Maria Felton Lowry, PharmD, BCPS, BCGP
Assistant Professor
University of Pittsburgh School of Pharmacy, Department of Pharmacy and Therapeutics
Palliative Care Clinical Pharmacy Specialist
UPMC Palliative and Supportive Institute

Cell: 412-627-8473
Office: 412-864-2899
Email: lowrymf@upmc.edu

If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

Dexmedetomidine for Terminal Delirium

Background:

Dexmedetomidine (Precedex®) is widely used in ICU for its anesthetic and sedative properties. Studies have shown its efficacy in decreased postoperative delirium when used prophylactically.[1] However, there has only been a few case studies that have explored the use of dexmedetomidine in palliative care.[2-5] Its positive effects as an anti-delirious agent[6], along with its light sedative properties make dexmedetomidine a potential candidate for managing terminal hyperactive delirium at the end of life.

Importance:

Despite the lack of new evidence in the management of terminal delirium, the current practice has been stagnated with the use of antipsychotics or benzodiazepines. Exploring potential new agents may increase palliative clinicians' therapeutic options that may target different hyperactive symptoms.

The Literature:

Palliative Medicine. 2021 Feb 17;35(4):729-737.

Hyperactive delirium at the end of life: An open-label single arm pilot study with dose escalation in adult patients admitted to an inpatient palliative care unit

Methods: Prospective, uni-center, dose escalation, single arm pilot study (n=22) patients diagnosed with delirium with hyperactive symptoms with predicted survival of <7 days.

- All patients start with Tier 1 (0.3mcg/kg/h) then if daily MDAS ≥13, dose escalation to Tier 2 (0.6mcg/kg/h) on continuous subcutaneous injection.
- Medical staff performs daily Memorial Delirium Assessment Scale (MDAS) 1h before infusion & 4h post dose escalation.
- Nursing staff performs Nursing Delirium Screening Scale (Nu-DESC) and Richmond Agitation Sedation Scale – Palliative Version (RASS-PAL) every 8h daily.

Objectives: To describe the effect of continuous subcutaneous infusion dexmedetomidine on delirium and sedation in patients with terminal delirium.

Outcomes:

- Primary: Severity of delirium assessed by daily MDAS, rousability measured by a RASS-PAL score
- Secondary: Opioid use for pain

Results:

Progression (n=22)		
Continued dexmedetomidine until death		11
Stopped as clinically improved		1
Transitioned to Standard of Care		10
Dose Escalation (n)		
Remained in Tier 1		9
Dose escalation to Tier 2		13
Primary Outcomes		
	Pre-initiation	Daily assessment
MDAS	13 - 22	2 - 12
RAAS-PAL	0 - 2	-4 - 0
Secondary Outcome (n)		
Required less opioid dose		2
Used same opioid dose		5
Required more opioid dose		15
Rescue medications usage (n)		
Benzodiazepines		14
Anticholinergics		4
Neuroleptics		1

- Most common adverse events: dry mouth (8 patients)
- Verbal interactions with medical/nursing staff were possible with 20 patients on Tier 1 and 8 patients on Tier 2.
- Only 1 patient reported discomfort (due to pain)
- With loved ones: 21 patients on Tier 1 and 11 patients on Tier 2

Discussion:

- This is the first reported pilot trial in the use of dexmedetomidine for terminal delirium.
- Compared to the pre-initiation of dexmedetomidine, every patient has reported improved MDAS and most patients reported improved RAAS-PAL score.
- Most of participating patient's ability to verbally communicate is important as two RCTs in the past have also demonstrated statistically significance in dexmedetomidine's ability to enable patient interaction when compared to midazolam and propofol in ICU.[7]
- No negative impact on survival after use of dexmedetomidine (median survival was 72.5h) as current literature suggests 24h as the mean survival duration for patients with terminal delirium.[8,9]
- Conclusions about efficacy cannot be made due to study design, lack of comparison arm, and the frequent need of pro-rata scoring of the MDAS.

Conclusion: Dexmedetomidine shows potential for the management of terminal delirium with improved interactivity.

Bottom Line:

- Clinical effectiveness of anti-delirium agents is difficult to conclude due to the challenging nature of assessing the severity of hyperactive delirium
  - Total MDAS score has been used to determine severity of delirium, although we cannot deduce which categories patients are scoring on which makes it difficult to assess if patients would have "required" sedation for terminal delirium (ie. agitation)
  - Does it matter if patients have disorientation or short-term memory impairment?...
- Majority of the participants had increased need for opioids (n=15/22)… previous literature suggested statistically significant direct relationship between hyperactive terminal delirium and PRN use of opioids[10]…
- Cost is a barrier especially in the hospice setting as the retail price of IV dexmedetomidine is around $75/day for Tier 1 and $150/day for Tier 2 patients, whereas other anti-delirious agents such as haloperidol or lorazepam cost less than 1/10 of this[11]
- When the goal of terminally ill and delirious patients and their family focuses on rousable sedation, dexmedetomidine could be considered as most of the patients were able to have verbal communications with both medical staff and their loved ones

CLINICAL PEARL: Dexmedetomidine (Precedex®) could be considered in terminally ill patients with hyperactive delirium when the goal of care focuses on verbal communication with their loved ones, although barriers exist to utilization in clinical practice

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CLINICAL PEARL: Dexmedetomidine (Precedex®) could be considered in terminally ill patients with hyperactive delirium when the goal of care focuses on verbal communication with their loved ones, although barriers exist to utilization in clinical practice